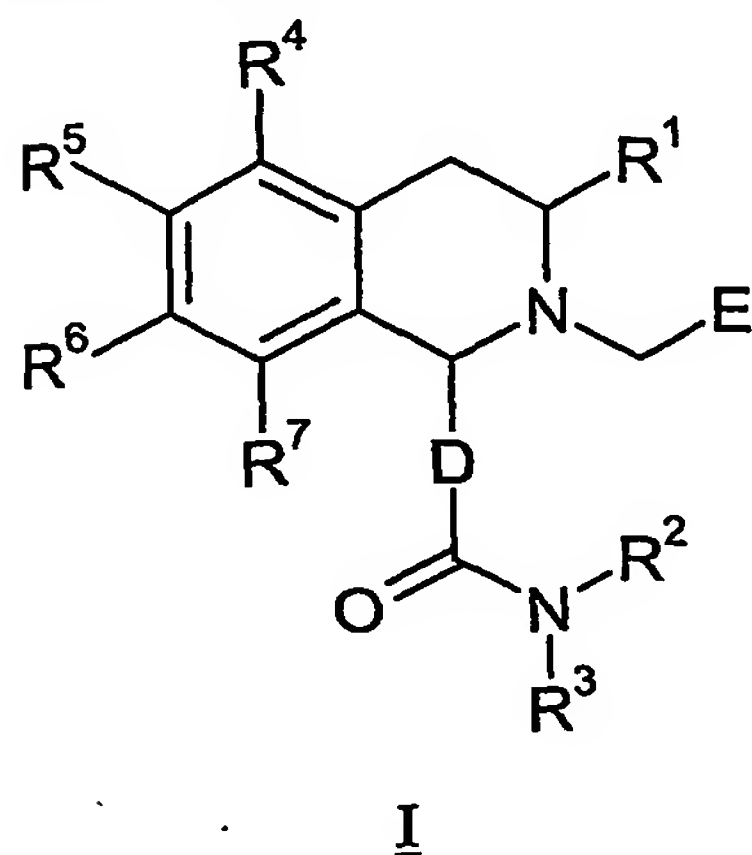


What is claimed is:

1. A compound of formula I, a pharmaceutically acceptable salt thereof, diastereomers, enantiomers, or mixtures thereof:



wherein

$R^1$  is selected from  $-H$  and  $C_{1-6}$ alkyl;

$R^2$  and  $R^3$  are independently selected from  $-H$  and  $C_{1-6}$ alkyl;

- 10  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocyclyl-oxy,  $C_{3-6}$ heterocyclyl- $C_{1-4}$ alkoxy,  $C_{6-10}$ aryl-oxy,  $C_{6-10}$ aryl- $C_{1-4}$ alkoxy,  $C_{1-6}$ alkyl- $S(=O)_2-O-$ ,  $C_{6-10}$ aryl- $S(=O)_2-O-$ ,  $C_{1-6}$ alkyl-NH- $S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$ ; or any two adjacent groups selected from  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  form a portion of a 5 or 6-
- 15 membered ring that fused with the benzene ring of formula I, wherein said  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocyclyl-oxy,  $C_{3-6}$ heterocyclyl- $C_{1-4}$ alkoxy,  $C_{6-10}$ aryl-oxy,  $C_{6-10}$ aryl- $C_{1-4}$ alkoxy,  $C_{1-6}$ alkyl- $S(=O)_2-O-$ ,  $C_{6-10}$ aryl- $S(=O)_2-O-$ ,  $C_{1-6}$ alkyl-NH- $S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected from halogen,  $C_{1-3}$ alkoxy,  $-OH$ ,  $-NO_2$ ,  $C_{1-3}$ alkyl,
- 20  $-NH_2$ , and  $-CO_2-C_{1-3}alkyl$ ;

E is a 5-membered heterocyclyl optionally substituted with one or more groups selected from halogen,  $C_{1-6}$ alkyl,  $-C(=O)-O-C_{1-6}alkyl$ ,  $C_{6-10}aryl$ ,  $C_{6-10}aryl-C_{1-4}alkyl$ , and  $C_{6-10}aryl-S(=O)_2-$ ; and

D is a divalent group comprising a benzene ring.

25

2. A compound according to claim 1; wherein

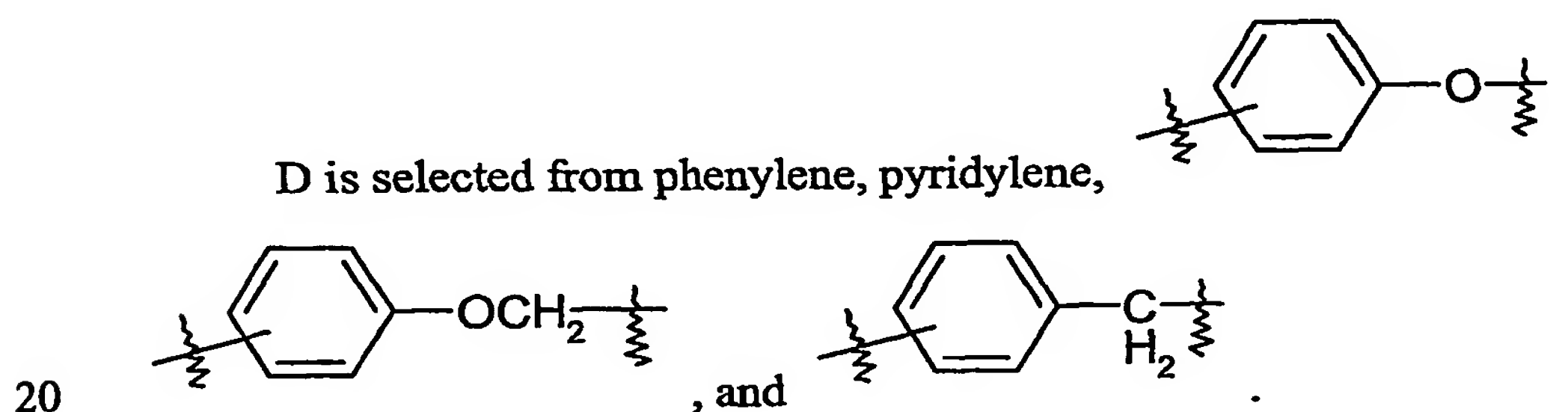
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$R^1$  is selected from  $-H$  and  $C_{1-3}alkyl$ ;

$R^2$  and  $R^3$  are independently  $C_{1-3}alkyl$ ;

$R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,  $C_{1-6}alkyl$ , phenyl,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ , tetrahydropyranyloxy, pyridinyloxy, morpholinyl-  
 5 morpholinyl- $C_{1-4}alkoxy$ , pyridinyl- $C_{1-4}alkoxy$ , morpholinyl- $C_{1-4}alkoxy$ , phenoxy, benzyloxy,  $C_{1-6}alkyl-S(=O)_2-O-$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-3}alkyl)_2N-S(=O)_2-O-$ ; or any two adjacent groups selected from  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  form a divalent group selected from  $-O-CH_2-O-$  and  $-O-CH_2-CH_2-O-$ , wherein said  $C_{1-6}alkyl$ , phenyl,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ ,  
 10 tetrahydropyranyloxy, pyridinyloxy, morpholinyl- $C_{1-4}alkoxy$ , tetrahydropyranyloxy, pyridinyl- $C_{1-4}alkoxy$ , morpholinyl- $C_{1-4}alkoxy$ , phenoxy, benzyloxy,  $C_{1-6}alkyl-S(=O)_2-O-$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-3}alkyl)_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected from halogen, methoxy,  $-OH$ ,  $-NO_2$ , and  $C_{1-3}alkyl$ ;

15 E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen,  $C_{1-4}alkyl$ ,  $-C(=O)-O-C_{1-3}alkyl$ , phenyl, benzyl, and benzenesulfonyl; and



3. A compound according to claim 1,  
 wherein

$R^1$  is selected from  $-H$  and methyl;

25  $R^2$  and  $R^3$  are selected from ethyl and isopropyl;

$R^4$ ,  $R^5$  and  $R^6$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,

$C_{1-6}alkyl$ , phenyl,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ , tetrahydropyranyloxy, pyridinyloxy, morpholinyl-  
 morpholinyl- $C_{1-4}alkoxy$ , pyridinyl- $C_{1-4}alkoxy$ , morpholinyl- $C_{1-4}alkoxy$ , phenoxy, benzyloxy,  $C_{1-6}alkyl-S(=O)_2-O-$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}alkyl-$

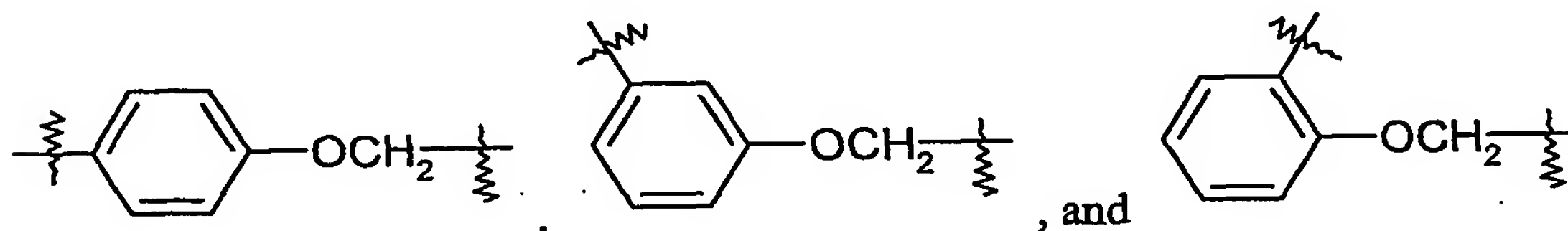
$C_{1-4}alkoxy$ , phenoxy, benzyloxy,  $C_{1-6}alkyl-S(=O)_2-O-$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}alkyl-$

NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-3</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> form -O-CH<sub>2</sub>-O-, wherein said phenoxy, benzyloxy, and phenyl-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen and methoxy;

5 R<sup>7</sup> is selected from -H and C<sub>1-3</sub>alkoxy;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen, C<sub>1-4</sub>alkyl, -C(=O)-O-C<sub>1-3</sub>alkyl, phenyl, benzyl, and benzenesulfonyl; and

10 D is selected from *para*-phenylene, *para*-benzylene,



4. A compound according to claim 1, wherein

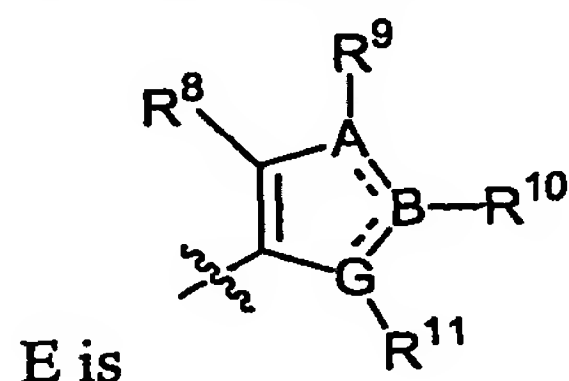
R<sup>1</sup> is selected from -H and methyl;

15 R<sup>2</sup> and R<sup>3</sup> are ethyl;

R<sup>4</sup> is selected from -H, NO<sub>2</sub> and methoxy, R<sup>5</sup> is selected from -H, -Br, -F, -OH, methoxy, methylsulfonyloxy, N,N-dimethylsulfamyloxy, and R<sup>6</sup> is selected from -H, -OH, -NO<sub>2</sub>, methoxy, ethoxy, isopropoxy, neopentyloxy, cyclobutyloxy, 4-tetrahydro-2H-pyranyloxy, 2-(4-morpholino)ethoxy, benzyloxy, phenoxy, 4-fluorophenoxy, 3-methoxyphenoxy, 4-methoxyphenoxy, 3-pyridinyloxy, methanesulfonyloxy, benzenesulfonyloxy, dimethylsulfamyloxy; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> form -O-CH<sub>2</sub>-O-;

20

R<sup>7</sup> is selected from -H and methoxy;

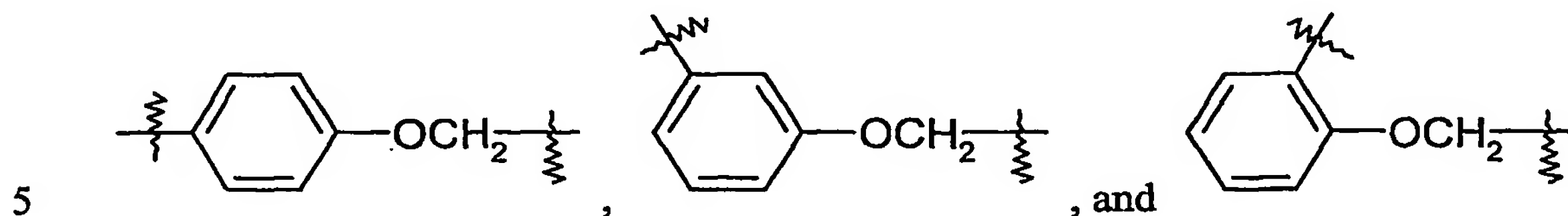


E is , wherein A and B are independently selected from C, N

25 and S, and G is selected from C, N, O and S with a proviso that at least one of A, B and G is C, at most one of A, B and G is S and one of the bonds between A and B, and between B and G is a double bond;

wherein  $R^8$  is selected from  $-H$ ,  $-Cl$ , methyl,  $-CO_2Me$  and phenyl;  $R^9$  is selected from  $-H$  and methyl;  $R^{10}$  is selected from  $-H$ , methyl, n-butyl and phenyl;  $R^{11}$  is selected from  $-H$ , methyl, benzyl and benzenesulfonyl.

D is selected from *para*-phenylene, *para*-benzylene,



5. A compound selected from:

COMPOUND 12.1.1: N,N-Diethyl-2- {[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} benzamide

10 COMPOUND 12.1.2: 2- {[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} -N,N-diethylbenzamide

COMPOUND 12.1.3: N,N-Diethyl-3- {[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} benzamide

15 COMPOUND 12.1.4: 3- {[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} -N,N-diethylbenzamide

COMPOUND 12.1.5: N,N-Diethyl-4- {[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} benzamide

COMPOUND 12.1.6: 4- {[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy} -N,N-diethylbenzamide

20 COMPOUND 12.1.7: 2- ({6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methoxy) -N,N-diethylbenzamide

COMPOUND 12.1.8: 4- ({6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methyl) -N,N-diethylbenzamide

25 COMPOUND 12.1.9: 4- {6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl} -N,N-diethylbenzamide

COMPOUND 12.1.10: N,N-Diethyl-4- {6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl} benzamide

COMPOUND 12.1.11: N,N-Diethyl-4- {7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl} benzamide

COMPOUND 12.1.12: N,N-Diethyl-4-{2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.13: 4-{2-[(2-Butyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

5 COMPOUND 12.1.14: 4-{2-[(2-Butyl-4-chloro-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.15: 4-{6,7-Dimethoxy-2-[(2-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

10 COMPOUND 12.1.16: 4-{6,7-Dimethoxy-2-[(3-phenyl-1H-pyrazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.17: 4-(6,7-Dimethoxy-2-{[1-(phenylsulfonyl)-1H-pyrrol-2-yl]methyl}-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 12.1.18: N,N-Diethyl-4-{2-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

15 COMPOUND 12.1.19: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.20: 4-{5,8-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

20 COMPOUND 12.1.21: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 12.1.22: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.23: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

25 COMPOUND 12.1.24: 4-{6,7-Dimethoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.25: N,N-Diethyl-4-{6-methoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

30 COMPOUND 12.1.26: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.27: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide



COMPOUND 12.1.28: 4-{2-[(1-Benzyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.29: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

5 COMPOUND 12.1.30: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.31: 4-({6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methoxy)-N,N-diethylbenzamide

10 COMPOUND 12.1.32: 4-({6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methyl)-N,N-diethylbenzamide

COMPOUND 12.1.33: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.34: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

15 COMPOUND 12.1.35: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.36: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

20 COMPOUND 12.1.37: 4-{2-[(2,5-Dimethyl-1,3-thiazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.38: 4-{6,7-Dimethoxy-2-[(2-phenyl-1,3-thiazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.39: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 12.1.40: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(2-morpholin-4-ylethoxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.41: 4-{7-Ethoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

30 COMPOUND 12.1.42: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.43: N,N-Diethyl-4-{6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.44: N,N-Diethyl-4-{7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.45: Methyl 5-[[1-{4-[(diethylamino)carbonyl]phenyl}-6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl]methyl]-1H-imidazole-4-carboxylate

5 COMPOUND 12.1.46: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl methanesulfonate

COMPOUND 12.1.47: N,N-Diethyl-4-{6-[(4-methyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

10 COMPOUND 12.1.48: N,N-Diethyl-4-{6-[(2-phenyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.49: 4-{6-Bromo-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

15 COMPOUND 12.1.50: 4-{6-Bromo-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.51: 4-{6,7-Dimethoxy-3-methyl-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.52: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

20 COMPOUND 12.1.53: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-7-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.54: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-5-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 12.1.55: N,N-Diethyl-4-{7-[(4-methyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.56: N,N-Diethyl-4-{7-[(2-phenyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.57: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

30 COMPOUND 12.1.58: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.59: 4-{7-(Cyclobutyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.60: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(neopentyloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

5 COMPOUND 12.1.61: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.62: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

10 COMPOUND 12.1.63: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl dimethylsulfamate

COMPOUND 13.1.1: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(tetrahydro-2H-pyran-4-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

15 COMPOUND 14.1.1: N,N-Diethyl-4-{6-methoxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.2: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

20 COMPOUND 14.1.3: N,N-diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.4: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.5: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 14.1.6: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(pyridin-3-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 15.1.1: 4-{7-(Benzyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

30 COMPOUND 16.4.1: N,N-Diethyl-4-{6-methoxy-7-(3-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.2: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide



COMPOUND 16.4.3: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl benzenesulfonate

COMPOUND 17.1.1: 4-{6,7-Dihydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 17.1.2: N,N-Diethyl-4-{6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.3: N,N-Diethyl-4-{7-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.4: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 17.1.5: N,N-Diethyl-4-{7-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.6: N,N-Diethyl-4-{6-hydroxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.7: N,N-Diethyl-4-{6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.8: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.9: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 18.1.1: 4-{2-[(1,4-Dimethyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 18.1.2: 4-{2-[(1,5-Dimethyl-1H-imidazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 19.1.1: 4-{7-Ethoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.1: 4-{(1S)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.2.1: 4-{(1R)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.2: N,N-Diethyl-4-[(1S)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.2.2: N,N-Diethyl-4-[(1R)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

5 COMPOUND 20.1.3: N,N-Diethyl-4-[(1S)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.2.3: N,N-Diethyl-4-[(1R)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

10 COMPOUND 20.1.4: N,N-Diethyl-4-[(1S)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.2.4: N,N-Diethyl-4-[(1R)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.1.5: N,N-Diethyl-4-[(1S)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

15 COMPOUND 20.2.5: N,N-Diethyl-4-[(1R)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.1.6: N,N-Diethyl-4-[(1S)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

20 COMPOUND 20.2.6: N,N-Diethyl-4-[(1R)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 20.1.7: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 20.2.7: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

25 COMPOUND 20.1.8: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 20.2.8: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide;

and pharmaceutically acceptable salts thereof.

30

6. A compound according to any one of claims 1-5 for use as a medicament.

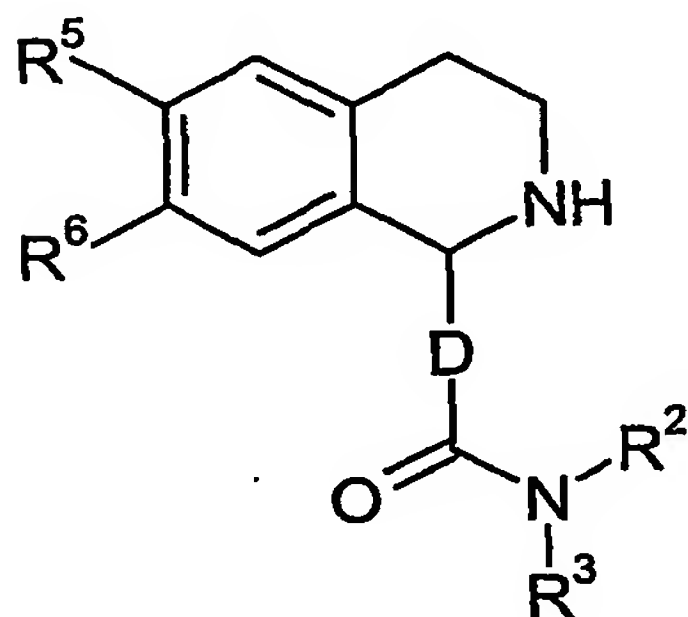
7. The use of a compound according to any one of claims 1-5 in the manufacture of a medicament for the therapy of pain, anxiety or functional gastrointestinal disorders.

8. A pharmaceutical composition comprising a compound according to any one of claims 1-5 and a pharmaceutically acceptable carrier.

9. A method for the therapy of pain in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to any one of claims 1-5.

10. A method for the therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to any one of claims 1-5.

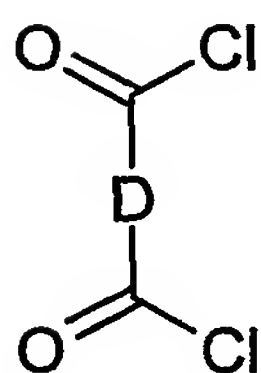
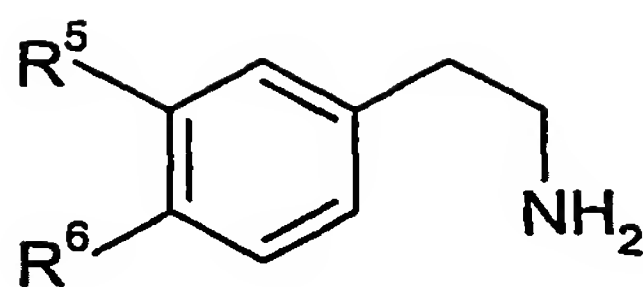
11. A process for preparing a compound of formula II,



II

comprising of the step of reacting a compound of formula III with a compound of formula IV in the presence of HNR<sup>2</sup>R<sup>3</sup>:

170

IIIIV

wherein

$R^2$  and  $R^3$  are independently selected from  $-H$  and  $C_{1-6}alkyl$ ;

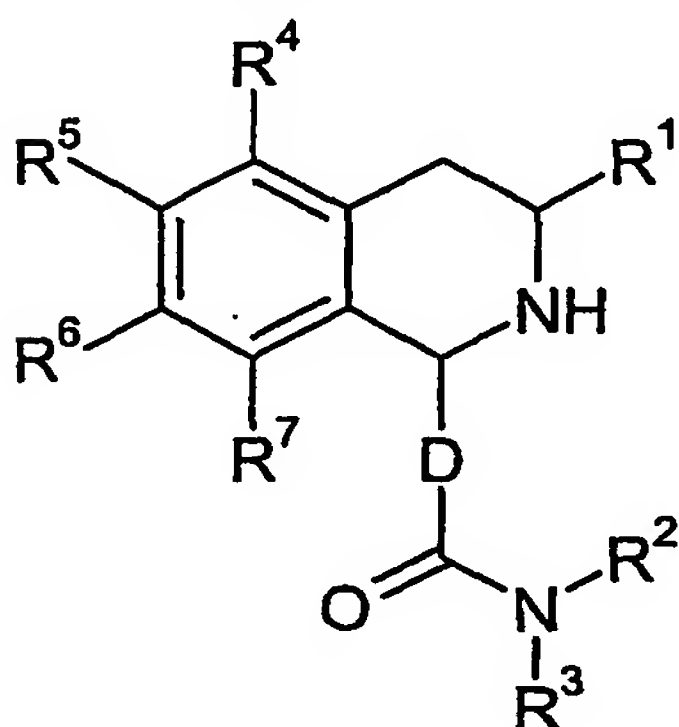
$R^5$  and  $R^6$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,  $C_{1-6}alkyl$ ,

- 5  $C_{6-10}aryl$ ,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ ,  $C_{3-6}heterocyclyl-oxy$ ,  $C_{3-6}heterocyclyl-C_{1-4}alkoxy$ ,  $C_{6-10}aryl-oxy$ ,  $C_{6-10}aryl-C_{1-4}alkoxy$ ,  $C_{1-6}alkyl-S(=O)_2-O-$ ,  $C_{6-10}aryl-S(=O)_2-O-$ ,  $C_{1-6}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$ ; or  $R^5$  and  $R^6$  together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said  $C_{1-6}alkyl$ ,  $C_{6-10}aryl$ ,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ ,  $C_{3-6}heterocyclyl-oxy$ ,  $C_{3-6}heterocyclyl-C_{1-4}alkoxy$ ,  $C_{6-10}aryl-oxy$ ,  $C_{6-10}aryl-C_{1-4}alkoxy$ ,  $C_{1-6}alkyl-S(=O)_2-O-$ ,  $C_{6-10}aryl-S(=O)_2-O-$ ,  $C_{1-6}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected from halogen,  $C_{1-3}alkoxy$ ,  $-OH$ ,  $-NO_2$ ,  $C_{1-3}alkyl$ ,  $-NH_2$ , and  $-CO_2-C_{1-3}alkyl$ ; and

D is a divalent group comprising a benzene ring.

15

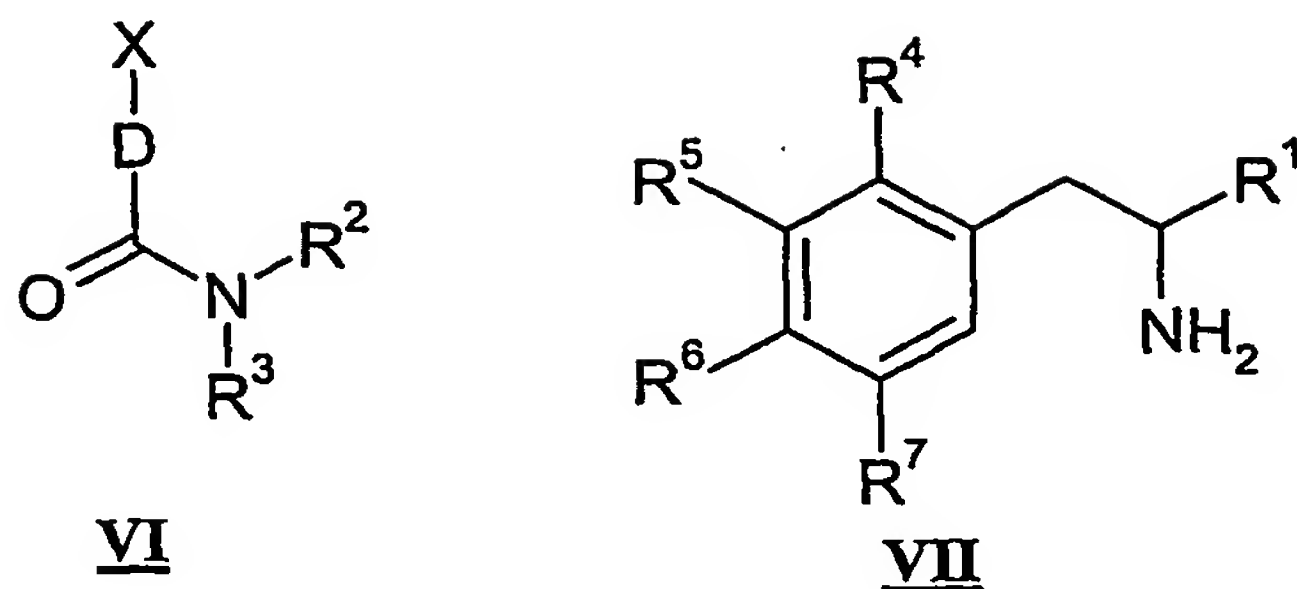
12. A process for preparing a compound of formula V,



V

comprising of the step of reacting a compound of formula VI with a

- 20 compound of formula VII in the presence of an acid catalyst:



wherein

X is selected from  $-\text{CH}(\text{OEt})_2$ ,  $=\text{CHOMe}$  and  $-\text{CHO}$ ;

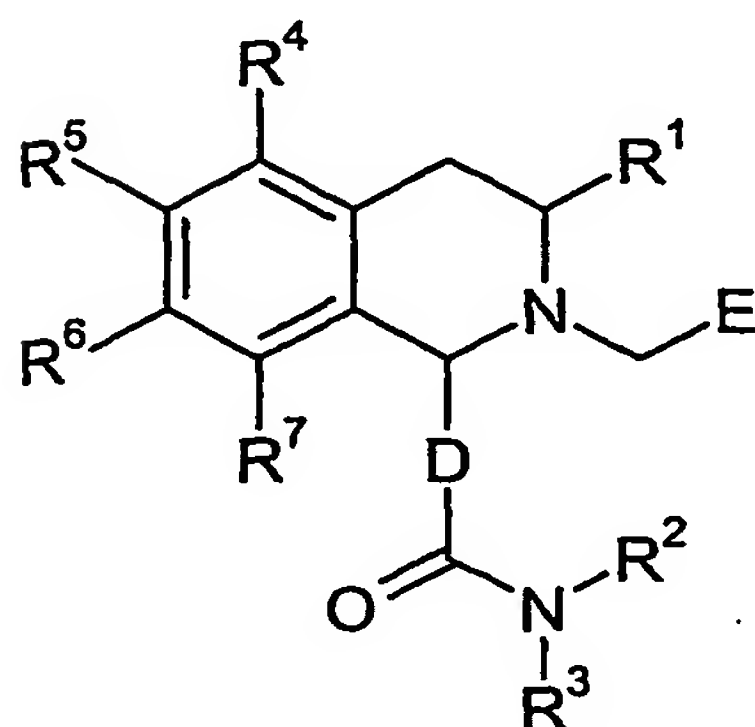
$\text{R}^1$  is selected from  $-\text{H}$  and  $\text{C}_{1-6}\text{alkyl}$ ;

$\text{R}^2$  and  $\text{R}^3$  are independently selected from  $-\text{H}$  and  $\text{C}_{1-6}\text{alkyl}$ ;

$\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$  and  $\text{R}^7$  are independently selected from  $-\text{H}$ ,  $-\text{OH}$ , halogen,  $-\text{NO}_2$ ,  $\text{C}_{1-6}\text{alkyl}$ ,  $\text{C}_{6-10}\text{aryl}$ ,  $\text{C}_{1-6}\text{alkoxy}$ ,  $\text{C}_{3-6}\text{cycloalkoxy}$ ,  $\text{C}_{3-6}\text{heterocyclyl-oxy}$ ,  $\text{C}_{3-6}\text{heterocyclyl-C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{6-10}\text{aryl-oxy}$ ,  $\text{C}_{6-10}\text{aryl-C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{1-6}\text{alkyl-S}(=\text{O})_2\text{-O-}$ ,  $\text{C}_{6-10}\text{aryl-S}(=\text{O})_2\text{-O-}$ ,  $\text{C}_{1-6}\text{alkyl-NH-S}(=\text{O})_2\text{-O-}$ , and  $(\text{C}_{1-6}\text{alkyl})_2\text{N-S}(=\text{O})_2\text{-O-}$ ; or any two adjacent groups selected from  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$  and  $\text{R}^7$  form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said  $\text{C}_{1-6}\text{alkyl}$ ,  $\text{C}_{6-10}\text{aryl}$ ,  $\text{C}_{1-6}\text{alkoxy}$ ,  $\text{C}_{3-6}\text{cycloalkoxy}$ ,  $\text{C}_{3-6}\text{heterocyclyl-oxy}$ ,  $\text{C}_{3-6}\text{heterocyclyl-C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{6-10}\text{aryl-oxy}$ ,  $\text{C}_{6-10}\text{aryl-C}_{1-4}\text{alkoxy}$ ,  $\text{C}_{1-6}\text{alkyl-S}(=\text{O})_2\text{-O-}$ ,  $\text{C}_{6-10}\text{aryl-S}(=\text{O})_2\text{-O-}$ ,  $\text{C}_{1-6}\text{alkyl-NH-S}(=\text{O})_2\text{-O-}$ , and  $(\text{C}_{1-6}\text{alkyl})_2\text{N-S}(=\text{O})_2\text{-O-}$  are optionally substituted with one or more groups selected from halogen,  $\text{C}_{1-3}\text{alkoxy}$ ,  $-\text{OH}$ ,  $-\text{NO}_2$ ,  $\text{C}_{1-3}\text{alkyl}$ ,  $-\text{NH}_2$ , and  $-\text{CO}_2\text{-C}_{1-3}\text{alkyl}$ ; and

D is a divalent group comprising a benzene ring.

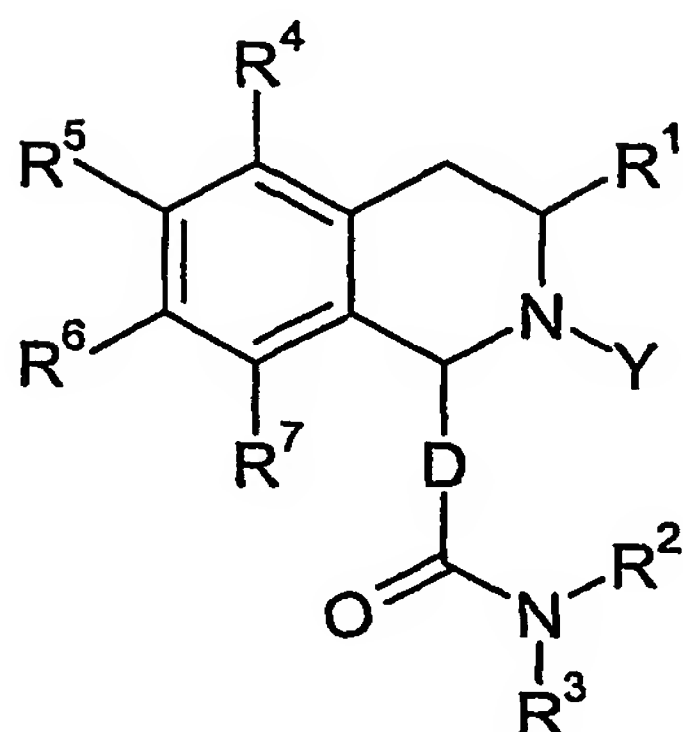
13. A process for preparing a compound of formula I,





I

comprising: reacting a compound of formula VIII with E-CHO:

VIII

5 wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R<sup>1</sup> is selected from -H and C<sub>1-6</sub>alkyl;

R<sup>2</sup> and R<sup>3</sup> are independently selected from -H and C<sub>1-6</sub>alkyl;

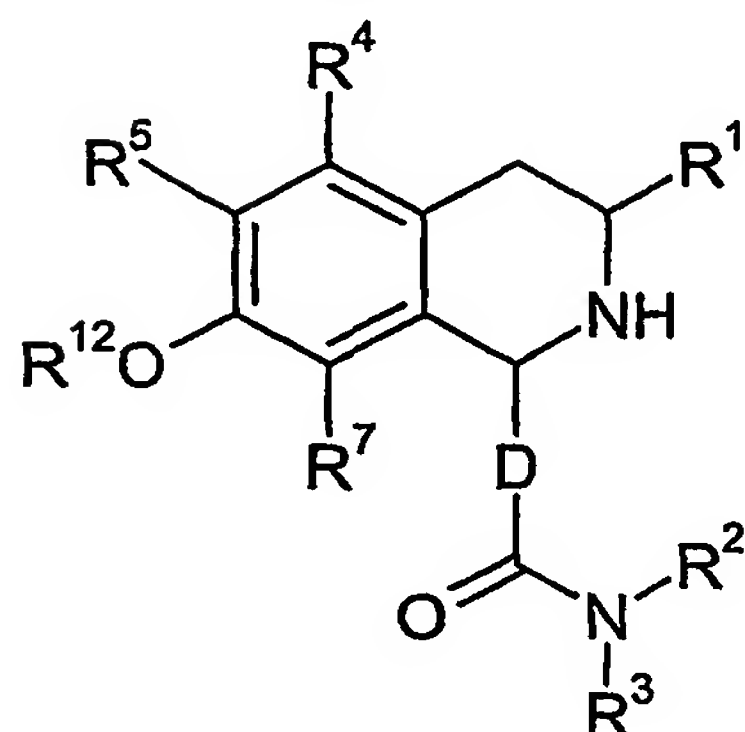
R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from -H, -OH, halogen, -NO<sub>2</sub>,

10 C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C<sub>1-6</sub>alkyl, 15 C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub>, and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl;

20 E is a 5-membered heterocyclyl optionally substituted with one or more groups selected from halogen, C<sub>1-6</sub>alkyl, -C(=O)-O-C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkyl, and C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-; and

D is a divalent group comprising a benzene ring.

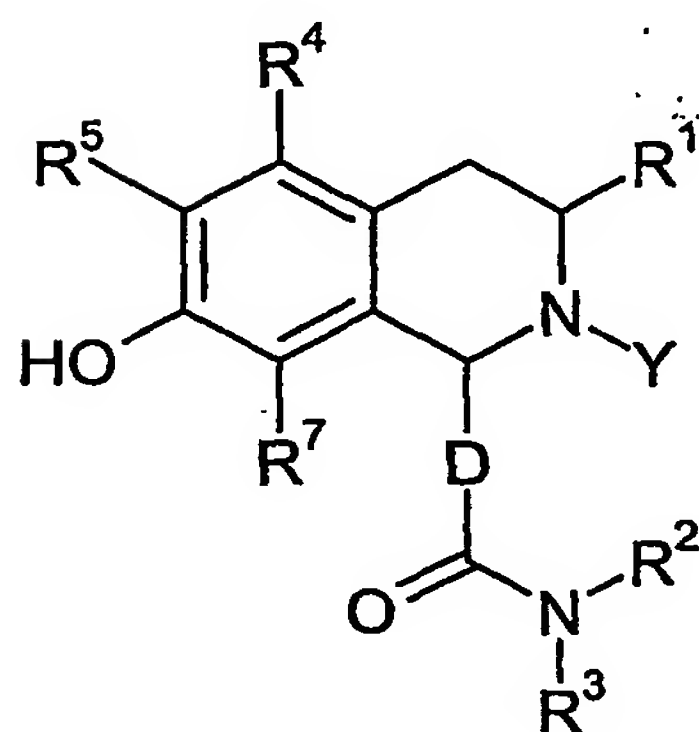
14. A process for preparing a compound of formula IX,



IX

comprising: reacting a compound of formula X with  $R^{12}$ -OH or  $R^{12}$ -B(OH)<sub>2</sub>:

5



X

wherein

Y is selected from -H and -C(=O)-O-t-butyl;

$R^{12}$  is selected from C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkyl,

10 C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkyl, C<sub>6-10</sub>aryl, and C<sub>3-6</sub>heteroaryl, wherein said C<sub>6-10</sub>aryl, C<sub>3-6</sub>heterocyclyl and C<sub>3-6</sub>heteroaryl are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub> and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl; and

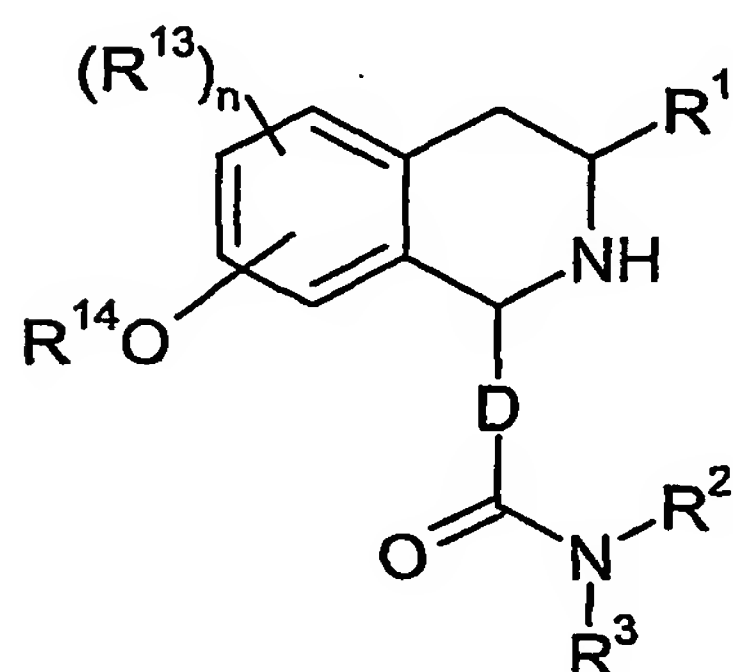
$R^1$  is selected from -H and C<sub>1-6</sub>alkyl;

15  $R^2$  and  $R^3$  are independently selected from -H and C<sub>1-6</sub>alkyl;

$R^4$ ,  $R^5$ , and  $R^7$  are independently selected from -H, -OH, halogen, -NO<sub>2</sub>, C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-,

- $C_{6-10}aryl-S(=O)_2-O-$ ,  $C_{1-6}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$ ; or  $R^4$  and  $R^5$  together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said  $C_{1-6}alkyl$ ,  $C_{6-10}aryl$ ,  $C_{1-6}alkoxy$ ,  $C_{3-6}cycloalkoxy$ ,  $C_{3-6}heterocyclyl-oxy$ ,  $C_{3-6}heterocyclyl-C_{1-4}alkoxy$ ,  $C_{6-10}aryl-oxy$ ,  $C_{6-10}aryl-C_{1-4}alkoxy$ ,  $C_{1-6}alkyl-S(=O)_2-O-$ ,  $C_{6-10}aryl-S(=O)_2-O-$ ,  $C_{1-6}alkyl-NH-S(=O)_2-O-$ , and  $(C_{1-6}alkyl)_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected from halogen,  $C_{1-3}alkoxy$ ,  $-OH$ ,  $-NO_2$ ,  $C_{1-3}alkyl$ ,  $-NH_2$ , and  $-CO_2-C_{1-3}alkyl$ ; and D is a divalent group comprising a benzene ring.

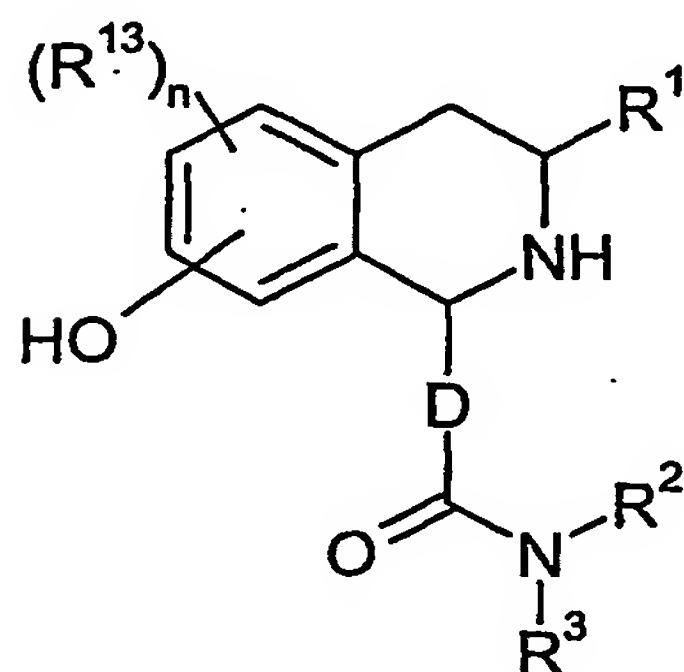
- 10 15. A process for preparing a compound of formula XI,



XI

comprising:

- reacting a compound of formula XII with  $NSCl$ ,  $NSBr$ , or  $(CF_3CO)_2O$  to protect the  $=NH$  group of formula XI;
- 15 reacting the protected compound with  $R^{14}-Y^1$  followed by deprotecting the  $=NH$  group:



XII

wherein

n is 0, 1, 2 or 3;

each  $R^{13}$  is independently selected from -H, -OH, halogen, -NO<sub>2</sub>, C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent  $R^{13}$  form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub>, and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl;;

$Y^1$  is halogen;

$R^{14}$  is selected from C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-;

$R^1$  is selected from -H and C<sub>1-6</sub>alkyl;

$R^2$  and  $R^3$  are independently selected from -H and C<sub>1-6</sub>alkyl; and

D is a divalent group comprising a benzene ring.